REMARKS:

Claims 12-17 are in the case and presented for consideration.

Claims 12, 13 and 17 have been amended to address the Examiner's objections found on page 2 of the above referenced Office Action.

Additionally, claim 13 has been further amended to address Examiner's rejection under 35 U.S.C. § 112, first paragraph so that all the claims are now believed to be in proper form.

First rejection under 35 U.S.C. § 103(a):

With respect to the Examiner's rejection of claim 12 under 35 U.S.C. § 103(a) found on page 3 of the Action, the article by Hampl et al. (hereinafter "Hampl") describes microspheres prepared from terpolymer of DL-lactic acid, glycolic acid and mannitol, copolymer of DL-lactic acid and mannitol and two lactido-glycolide copolymers by solvent evaporation emulsion technique. Similarly prepared microspheres are described in the article by Chen et al. (hereinafter "Chen").

Generally, the microspheres represent release systems having a particle structure wherein the individual fractions of the active matter contained in the individual microspheres are discretely separated from each other by either a gaseous phase (air) if administered on their own or a liquid medium if administered as a liquid formulation. Moreover, the microspheres have incorporated in their surface sheet a polymer emulsifier and residual solvents and each microsphere in addition shows a heterogeneous structure composed of globe cavities produced by drying out an inner aqueous phase.

In contrast, the present invention as defined in claim 12 is a plastic (or ready to be

rendered plastic) monolithic, i.e. non-particulate system (see: homogeneous one-phase solution, micellar colloid system, one-phase or two-phase gel, suspension, paste or emulsion). The term "monolithic" was added to claim 12 in order to further clarify this important distinction.

As a result, the active matter in the present invention is directly and without any barrier scattered in a carrier (biodegradable oligoester). Therefore, the composition of claim 12 can be prepared merely by heating the active matter in the presence of the carrier. Thus both Hampl and Chen are structurally very different from the present invention.

An additional important distinction is that both Hampl and Chen have a different release mechanism than that of the present invention. The monolithic system is recognized to swell and degrade by the hydrolysis of the ester bonds which produces both hydroxyl and carboxyl groups. The acid degradation products catalyse further degradation of the system. Such an autocatalytic impact of the degradation products on acid hydrolysis is influenced by their stay in the oligoester system. The stay time of the degradation products in the system is, completely, dependent on the size of the system.

As a result of the very small size of the microspheres in Hampl and Chen their release systems are different. The hydrolysis of these microspheres systems proceeds without the catalytic effect of the above-mentioned degradation products. Thus, in Hampl and Chen the release of active matter is influenced to a greater degree by their physico-chemical properties, such as solubility, distribution coefficient, sorption, and ionisation. This greater influence of the physico-chemical properties on the release kenetics in Hampl and Chen is due to the shorter diffusion path of the molecules or ions

of the active matter, which in microsphere systems is shorter by a factor of 2 to 3.

Second rejection under 35 U.S.C. § 103(a):

The Examiner has rejected claims 13-17 under 35 U.S.C. § 103(a) as being obvious from Hampl in view of Chen and taken further in view of U.S. Patent 5,783,205 to Berggren et al. (hereinafter "Berggren"). This rejection of claims 13-17, found on page 7 of the Action, is respectfully traversed because claim 12 in believed to be unobvious over the combination of Hampl in view of Chen for the reasons detailed above, so that claims 13-17 are also believed to be unobvious.

Additional reasons for the unobviousness of claims 13-17 over the cited combination also exist, however.

U.S. Patent 5,783,205 to Berggren et al. (hereinafter "Berggren") provides a matrix material which can be used to deliver a drug, such as an antibiotic, into a diseased tissue pocket, such as a periodontal pocket. The material is preferably a boidegradable oligomer or polymer. The oligomer or polymer containing the drug is heated and is than delivered, preferably by injection, into the tissue pocket at a physiologically compatible temperature. Once the bioerodible material is injected into the pocket, the material cools to the body temperature of the pocket. As it cools, the material hardens and remains in place within the tissue pocket. The hardened material bioerodes in the pocket and releases the drug over a period of several days. Berggren also mentions that a "[f]urther preferred group useful as matrix materials are oligomers of glycolic acid and/or lactic acid and their derivatives with mono- and/or polyfuncional alcohols." (col. 7 ln. 25-27).

As the only specific method for preparing those preferred matrix materials, Berggren teaches a synthesis from cyclic esters of lactic acids (lactones) realized by

polymerizing lactones while opening their cycle. (col. 6 ln. 57-58).

By contrast, the biodegradable oligoesters in present claims 12 to 17 are expressly prepared by polycondensation reaction of polyhydric alcohol containing at least 3 hydroxy groups with at least one aliphatic a-hydroxy acid (see claim 12). This preparation method produces different quality final products than that of the preparation method in Berggren.

Firstly, the synthesis from the cyclic ester taught in Berggren consists of polymerizing the cyclic ester while opening the cycle thereof as already mentioned above. The polymerization is the reaction that proceeds spontaneously and finishes by a termination. In comparison with the product obtained by the polymerization of the present invention, the products obtained by the polymerization taught in Berggren show a broader distribution of molecular weights and a different (more random) arrangement of the constituent units in the copolymers. In the polycondensation reaction of the present invention both the distribution and arrangement can be controlled by terminating the reaction when desired parameters are reached.

Secondly, the products of the polymerization in Berggren contain a high proportion of non-reacted monomers that considerably influence the properties of the matrix materials. This includes the autocatalytic impact on the running of the biodegradation of the matrix material. Namely, the content of the monomers and low molecular water-soluble components is very high. These undesirable substances must therefore be withdrawn, usually by precipitating them from the solution. However, this precipitation undesirably influences the polydispersity of the matrix material since along with the monomers also a portion of the matrix material is eliminated. In addition, when precipitating, the matrix materials are contaminated with the used solvents the elimination of which is not possible. These problems are not encountered when using the biodegradable oligoesters of the

present invention.

Thirdly, as distinct from the biodegradable oligoesters of the present invention, the matrix materials of Berggren prepared by the cycle-opening polymerisation in the presence of the polyhydric alcohols exhibit a low branching rate when having a low molecular weight. In such a case, the cyclic lactones react with the polyhydric alcohols, optionally with the acids. The polyhydric alcohols function as initiators as in pentaerythritol [Helminen, A., Korhonen, H., Seppala, J. V., Polymer 42 (2001 3345]. With the lower branching rate of the oligomers used in Berggren the resulting oligoester material shows lower content of end hydroxyl groups. The end hydroxyl groups play key role in the mechanism of the degradation of the matrix carrier and thus influence the kinetics of the release of the active matter [De Jong, S.J. et al., Polymer 42 (2001),2795]. No such effect occurs with the biodegradable oligoesters of the present invention.

In light of the aforementioned, it is believed to be clear that the composition of present claims 12 through 17 comprised as a matrix carrier which is structurally and with respect to the presence of accompanying substances, different from the carrier material disclosed in Berggren.

Finally, the matrix material of Berggren is to be administered topically into open periodontal, ophthalmic, or vaginal pockets. By contrast, the present composition is designed for intratissue administration. Compositions designed for topical administration generally exhibit release profiles which are quite different from that of compositions designed for intratissue administration. Thus, a person skilled in the art would not have though to use the teaching of Berggren in a composition designed primarily for intratissue administration.

Accordingly, the application and claims are believed to be in condition for allowance, and favorable action is respectfully requested.

No new matter has been added.

If any issues remain, the Examiner is respectfully invited to contact the undersigned at the number below, to advance the application to allowance.

Respectfully submitted,

/SALVATORE P SPEZIO/
Salvatore P. Spezio
Reg. No. 60,868
Attorney for Applicants
(845) 359-7700

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NOTARO & MICHALOS P.C.
100 Dutch Hill Road, Suite 110
Orangeburg, New York 10962-2100

Customer No. 21706

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